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Pursuant to 37 C.F.R. § 1.121(b)(1)(ii)

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METHODS FOR DECREASING BETA AMYLOID PROTEIN

Cross-Reference to Related Applications

This application is a divisional of pending prior application U.S. Serial
No. 09/239,387 filed January 28, 1999, which is a divisional of U.S. Serial
 5 No. 09/046,235 filed March 23, 1998, now U.S. Patent No. 6,080,778. The
United States government has certain rights in this invention by virtue of
National Institutes of Health grant number RO1NS33325 to Bruce A. Yankner.

Background of the Invention

[The United States government has certain rights in this invention by
 10 virtue of National Institutes of Health grant number RO1NS33325 to Bruce A.
 Yankner.]

Alzheimer's disease (AD) is the most common cause of dementia in the
 aged population. The accumulation of large numbers of senile plaques
 containing the 40-42 amino acid amyloid β protein ($A\beta$) is a classic pathological
 15 feature of AD. Both genetic and cell biological findings suggest that the
 accumulation of $A\beta$ in the brain is the likely cause of AD (Yankner, B.A. (1996)
 Neuron 16, 921-932.; Selkoe, D.J. Science 275, 630-631 (1997)). Strong
 genetic evidence in support of the pathogenic role of $A\beta$ came from the
 observation that individuals who inherit mutations in the amyloid precursor
 20 protein almost invariably develop AD at an early age. These mutations increase
 the production of a long variant of the $A\beta$ peptide that forms senile plaques in
 the brain (Goate et al., (1991) Nature 349, 704-706). Mutations and allelic
 variations in other genes that cause AD, including the presenilins and
 apolipoprotein E, also result in increased production or deposition of the $A\beta$
 25 peptide. Reiman, et al. (1996) N.E.J.Med. 334, 752-758, reported that in middle
 age, early to mid 50's, individuals who are homozygous for the Apo E4 gene
 have reduced glucose metabolism in the same regions of the brain as in patients
 with Alzheimer's disease. These findings suggest that the pathological changes